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**Faculty of Science**

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# Neonatal cheiloplasty as the first surgery in patients with orofacial clefts, its benefits and possible risks

Neonatální cheiloplastika jako první operativa u pacientů s orofaciálními rozštěpy, její výhody a možná rizika

Bachelor´s thesis

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## Prohlášení

*Prohlašuji, že jsem závěrečnou práci zpracoval/a samostatně a že jsem uvedl/a všechny použité informační zdroje a literaturu. Tato práce ani její podstatná část nebyla předložena k získání jiného nebo stejného akademického titulu.*

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## Poděkování

Děkuji své školitelce doc. RNDr. Janě Velemínské, Ph.D. za zadané téma, průběžné poznámky k práci a veškerou poskytnutou pomoc. Za důkladnou korekturu a užitečné připomínky děkuji MUDr. Janu Strojilovi Ph.D. Děkuji všem, kteří mě při psaní této práce podporovali a pomáhali svými radami.

## Abstract

Neonatal cheiloplasty is the first plastic surgery performed in patients with orofacial clefts, usually carried out at the age of 1 to 8 days. A modified protocol for standard cheiloplasty, performed at the age of 3 to 6 months, is used.

Neonatal cheiloplasty is currently a predominant method for lip surgery in cleft lip patients in the Czech Republic. Advantages of this method are better scar healing associated with better aesthetic results, reduced psychological and sociological pressure on the family and the infant, better quality of feeding and breastfeeding, and possibly reduced need of secondary repair. There is no documented direct negative consequence of the early timing. Nevertheless, possible risks can be associated with general anaesthesia at such low age, as it could have a negative effect on future IQ of the patient, and a possibility of reduced growth and development of jaws and impaired facial aesthetic outcomes. Further, compared to classical cheiloplasty, early surgery is more expensive and demands higher skills and experiences of the surgeon and the whole team performing the procedure.

Main goals of this work were to evaluate the benefits and possible risks of neonatal cheiloplasty as the first surgery performed in patients with orofacial clefts using available studies on this topic and to discuss, on which topics further research should focus.

**Keywords:** neonatal cheiloplasty, cleft lip, cleft lip and palate, operation in new-borns, early surgery, operation timing

## Abstrakt

Neonatální cheiloplastika je první plastickou operací prováděnou u pacientů s orofaciálními rozštěpy, obvykle ve stáří 1 až 8 dní. Používá se modifikovaný protokol pro cheiloplastiku, standardně prováděnou ve věku pacienta 3 až 6 měsíců.

V České republice se momentálně jedná o převládající metodu operace pacientů trpícími rozštěpem rtu. Mezi výhody této operace patří lepší hojení jizvy a lepší estetické výsledky, snížený psychický a sociální tlak na rodinu a dítě, možnost normálního krmení či kojení novorozence od raného věku a nižší pravděpodobnost potřeby sekundárních operací. Negativní následky způsobené přímo načasováním operace nejsou dokumentovány. Nicméně diskutované otázky zahrnují bezpečnost celkové anestezie a její vliv na budoucí IQ jedince, vliv na růst a vývoj čelistí a estetické výsledky zákroku. Zároveň, neonatální cheiloplastika představuje náročnější zákrok z finančního hlediska a klade zvýšené nároky na zkušenost celého chirurgického týmu.

Hlavním úkolem této práce bylo dle dostupné literatury zhodnotit výhody a možná rizika spojená s neonatální cheiloplastikou jako prvním chirurgickým zákrokem prováděným u pacientů s orofaciálními rozštěpy. Zároveň zmínit, na které problémy je zaměřený současný výzkum a která problematika by měla být sledována v budoucích studiích.

**Klíčová slova:** neonatální cheiloplastika, rozštěp rtu, rozštěp rtu a patra, načasování operace

## List of abbreviations

CL – cleft lip

CLO – cleft lip only

CP – cleft palate

CPO – cleft palate only

CLP – cleft lip and palate

CL/P – cleft lip with or without cleft palate

UCLP – unilateral cleft lip and palate

BCLP – bilateral cleft lip and palate

IQ – intelligence quotient

OME – otitis media with effusion

ENT – ears, nose and throat

EOT – extraoral traction

TF – Tennison flap

VF – vestibule deepening

NF – nasal passage

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# 1 Introduction

A cleft lip, together with cleft palate alone and cleft lip and palate, are different types of orofacial malformations. They are caused by various developmental and environmental factors. These developmental defects can potentially be a source for a wide range of serious health issues in patients, including hearing problems, poorly developed speech and complications in face morphology development.

The history of surgical corrections of cleft lip does not go very far. It was in the 19th century, also thanks to the introduction of first chloroform anaesthesia, when the development of more routine techniques could progress (Perko, 1986). The first mention of cleft lip closure comes from ancient China in 390 B.C. (Boo-Chai, 1966), and there are some rare mentions from the Middle Ages (Perko, 1986). Throughout history, people born disabled and with malformations were mostly avoided and despised, so any attempts to efficiently repair cleft lips were sparse, also in light of the absence of effective anaesthesia. Cleft palate surgery was avoided even more, as it was presumed to be a result of syphilis. There are some known protocols used to fix lip injuries, potentially also used for congenital cleft lip.

In the 19th century, various kinds of mucosal flaps were used with differing results, e.g. nasal mucosal flap or mucoperiosteal flap (which is still used in some places). A breakthrough in surgical technique was developed by Werner Hagedorn in the 19th century and the main principle of his procedure was later used as a base and modified into various alterations by other 20th century authors, such as Veau, LeMesurier, Tenisson, Randall, Millard and Pfeifer (Bill et al., 2006). Hagedorn managed to solve the problem of insufficient thickness of the medial part of the lip by using a quadrangular flap (Hagedorn, 1884).

The timing of the cheiloplasty, surgery of the cleft lip (both bilateral and unilateral types) is a widely debated topic. As early as the 17th century, it was mentioned by Hendrik van Roonhuyze, who recommended the age of a baby to be at least 3–4 months. The timing is set mainly to avoid the supposedly sensitive period of a freshly born infant. Nevertheless, it has been shown that operating new-borns in their first week of life may not carry additional risks, on the contrary, it may actually be beneficial. Healing abilities are reportedly at their peak right after birth. And while the aesthetic improvements of the scar are not fully agreed on, the feeding benefits are generally accepted. Breastfeeding is enabled right after the surgery; babies can develop a good sucking reflex, and that decreases the likelihood of malnutrition. Psychological bond between the mother and a child is also formed much more easily. Overall

influence on the family is assumed to be very positive. Parents can leave the hospital with a healthy-looking baby and early repair gives the new-born a good start into life and a good opportunity of managing this multifactorial issue safely and without additional consequences. However, one of the biggest dilemmas surgeons face is the paediatric anaesthesia. Determining how much it can affect brain development in this crucial period is a complex issue. It is yet to be confirmed if there are negative consequences for children undergoing surgery up to the age of several years, so to differentiate such a subtle variation caused by several months difference in timing, is an extremely delicate dispute. Further, children who suffer from both cleft lip and palate undergo the surgery of the palate only a few months after their cheiloplasty. This second anaesthesia has more influence on face morphology and jaws formation.

The goal of this paper is to evaluate what we know about the early surgical repair of a cleft lip as a whole and the effects on the patient, based on the choice of the timing. Another goal is to describe the current research areas and identify topics on which future research should focus.

# 2 Theoretical part

## 2.1 Orofacial malformations

### 2.1.1 Cleft prevalence

Incidence of orofacial clefts in the Caucasian population is around 1 in 700 live births but the number varies greatly geographically and with ethnicity (Mossey et al., 2009; Murray, 2002).

Data from the Czech Republic from years 1961–2000 report the incidence of orofacial clefts as 18.23 per 10,000 live born children (Sípek et al., 2002). Prevalence of CL is 2.09 per 10,000 and for CL/P 11.13 per 10,000 infants. A higher risk was observed in 15-year-old women and in those older than 35 years. Data collected between 1994–2008 report a prevalence of 1 in 600 live births (Urbanova et al., 2013). Incidence of isolated CL was calculated to be 0.39/1000 and is higher for males than females, the same applies to CLP patients, with an incidence of 0.57/1,000. Incidence of CP is 0.68/1,000 and female babies are slightly more affected than male infants. Varying prevalence of clefts was noted even between various Czech regions (the highest was measured in the Beroun district 2.86/1,000 and the lowest was 0.72/1,000 in the Svitavy district), which indicates possible differences caused by diverse harmful environmental factors (Peterka et al., 2000). Observations of monthly

differences in incidence were reported from multiple countries, including the Czech Republic. Data collected between 1964 and 2000 showed a seasonal difference in the prevalence of orofacial clefts (Peterka et al., 2018). Girls affected by clefts were born with higher frequency in the period from January to March, and boys from April to May. The period from May to October was estimated to be critical for clefts development. These findings show there could be some major factors (biological, physical, and chemical) influencing early stages of embryologic development, presumably associated with the warm season corresponding to the time of conception. A different incidence in different sexes was found when evaluating the genetic risk of babies with an affected parent. Affected babies of mothers with CL or CLP were dominantly boys, babies of mothers with CP girls. It was fairly similar for babies of fathers with clefts, except when fathers were suffering from CLP; then the distribution of sexes was even (Peterka et al., 1996).

### 2.1.2 Development of clefts

Clefts originating from the mouth and lips are the most common of the orofacial malformations (Eppley et al., 2005). These congenital defects are caused by the failure of cell migration during the $4^{th}$–$6^{th}$ week of the embryonic development. They are formed when segments forming palates are not properly fused. The outcome is a fissure along the midline, which can be complete or partial and it is often combined with a cleft lip. A cleft lip appears as the first one during the embryonic development, it occurs when the maxillary prominences are not properly connected with the fused medial nasal prominences (Moore and Reid, 1982). Cleft palate develops when the palatal shelves fail to fuse. The cleft types and how extensive the clefting is differ according to when precisely the disturbance of the fusion process starts, and how long it lasts (in *Fig. 1*). Cleft lip and palate, the most severe of the cleft types, occur when the disturbance lasts through the whole critical period.

Antenatal diagnosis of clefts is possible thanks to prenatal scanning, but malformations are not always noticed. The detection of malformations associated with cleft lip tends to be fairly sensitive, around 88%, but in the sample data, isolated cleft palate is never detected with ultrasound screening (Maarse et al., 2011).

Clefts can be caused by multiple factors, both environmental and genetic, and the interaction between these. Inheritance plays a major role and clefting is probably a result of interaction of several genes (Marazita and Mooney, 2004). Notable environmental conditions which increase the risk of non-syndromic clefts are maternal smoking (Carinci et al., 2003), alcohol

consumption (Werler et al., 1991), and poor nutrition during pregnancy, e.g. insufficient amount of folic acid (Werler et al., 1999). Gestational bleeding in the first trimester significantly increases the incidence of CLP while reducing the incidence of isolated CP (Peterka et al., 2012). Another reported risk factor is hyperthermia during the critical period of pregnancy (Shahrukh Hashmi et al., 2010). Rate of children born with isolated cleft lip or palate was higher for women who experienced fever during the first trimester, particularly for those who did not use antipyretics. Higher paternal age is also mentioned as a possible risk factor (Fraser and Calnan, 1961).

Statistics show that in terms of the sexes, males are two times more likely affected by CL and CLP than females, who on the contrary prevail in the group of patients with CP (Fraser and Calnan, 1961). A unilateral cleft lip is the most common cleft and predominantly occurs on the left side; it is much more frequent than bilateral cleft lip. A bilateral cleft lip is almost never present alone without a palatal cleft.

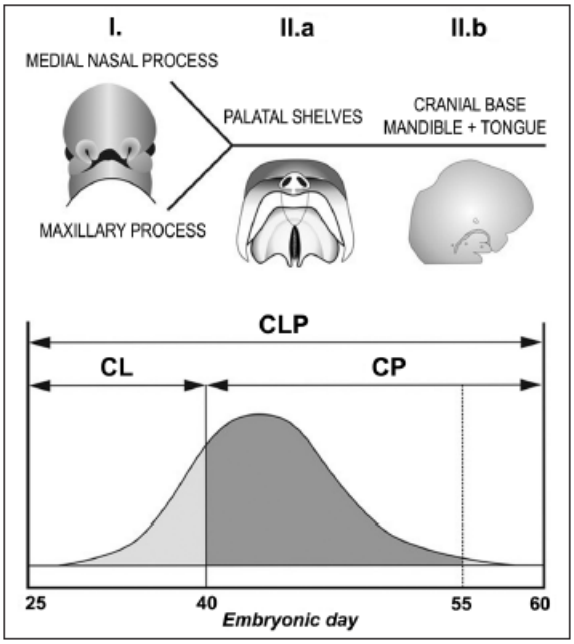


*Fig. 1. The critical period for development of orofacial clefts. CL – cleft lip; CP – cleft palate; CLP – total cleft lip and cleft palate. These cleft types originate during three critical periods of orofacial development – I., II.a, II.b; x-axis – the embryotic day of origin of particular cleft type; y-axis – the theoretic ratio of cleft types in embryos (Peterka et al., 2012).*

### 2.1.3 Classification of cleft lip and palate

Orofacial clefts are in principle ranked according to the extension of the cleft into three major classes: cleft lip only (CL, CLO), cleft of the soft/hard palate only (CP, CPO) and cleft lip

combined with cleft palate (CLP) (Peterka et al., 2012). All types can be bilateral (two complete clefts on both sides) or unilateral (only one side is clefted). Clefts can be complete, which in the case of cleft lip means that the nasal sill, the alveolus, and the lip are disrupted, or incomplete to various extents (see *Fig. 2*). Bilateral cleft lip occurs either as symmetric (both complete or incomplete) or asymmetric (one is complete and one incomplete). Nasal asymmetry is generally present even in incomplete and minor clefts.

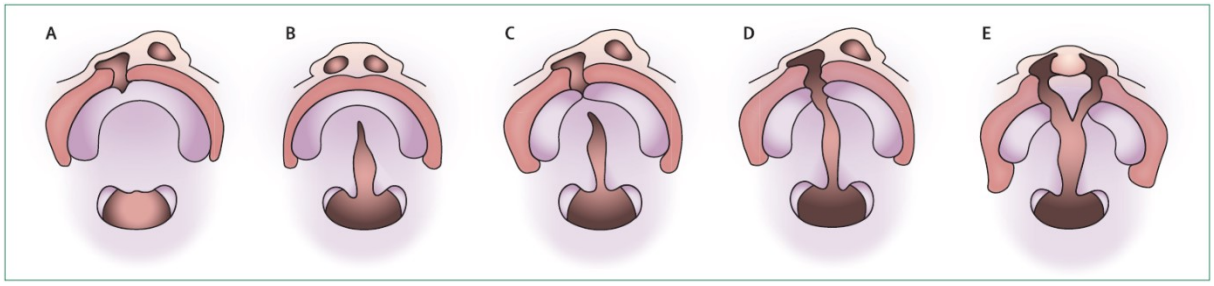


*Fig. 2. Types of non-syndromic orofacial clefts. (A) Cleft lip and alveolus. (B) Cleft palate. (C) Incomplete unilateral cleft lip and palate. (D) Complete unilateral cleft lip and palate. (E) Complete bilateral cleft lip and palate (Mossey et al., 2009).*

One of the first widespread methods of cleft classification was a simple system developed by Veau (Veau, 1931). Today, it is used sparsely as it does not include cleft lip only and incomplete clefts, but it is a practical way to divide clefts into some basic types. It establishes four groups of clefts: total unilateral (I) and bilateral (II) clefts of the lip and palate, clefts of the soft palate only (III) and clefts of the soft and hard palate (IV).

A more recent and detailed classification of various types of clefts used today comes from Kriens, who modified the previously proposed system (Kriens, 1987). This system is formed by the acronym LAHSHAL, where lip (L), alveolus (A), hard (H), and soft (S) palate are each represented by its own letter. Total clefts are symbolized by upper case, incomplete by lower case letters. Partial clefts of the hard palate are identified by hSh and complete clefts by HSH. This scheme also enables classification of unilateral and bilateral clefts. One of the "H" was later omitted, forming the shortcut "LAHSAL" (*Fig. 3.*) (Shah et al., 2011).

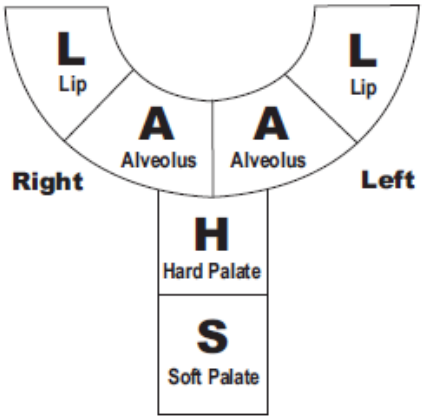


*Fig. 3. LAHSAL system divides the mouth into six major areas. Absence of a cleft is indicated by a dot. For lip and alveolus, right/left side is defined, the first letter belongs to the right lip. A complete cleft is specified with an upper case letter, incomplete with a lower case (Shah et al., 2011).*

### 2.1.4 Related health issues

Oral clefts are multifactorial defects affecting speech abilities, hearing, physical appearance, and psychology of an individual. They may cause long-lasting difficulties with social integration and health.

Clefts often occur as a part of syndrome or chromosomal anomaly; they can be linked to other developmental malformations (Kirschner and LaRossa, 2000). These syndromic clefts are more commonly associated with cleft palate. Syndromic orofacial clefts can be associated with Van der Woude's syndrome (or congenital fistula labii inferioris) (Van Der Woude, 1954), trisomy 13 syndrome, congenital double lip (Calnan, 1952), velo-cardiofacial syndrome (Goldberg et al., 1993) and others. Non-syndromic clefts are isolated facial clefts. Around 70% of CL/P are non-syndromic (Stanier and Moore, 2004).

Perinatal morbidity and mortality are reportedly higher in foetuses with facial clefts and the number significantly increases when there is an association with other anomalies (Ngai et al., 2005). Patients with orofacial clefts have their mortality increased within the first years of life and the risk remains higher than in the general population up to the age of 55 years (Christensen et al., 2004). Among reported reasons are all the major causes of death; increased frequency of suicides compared to unaffected population, and consequent health issues caused by an increased incidence of structural brain anomalies related to the abnormally low amount of cerebral white matter in clefts patients (Nopoulos et al., 2007).

### 2.1.5 Health consequences

Taking care of an infant affected by orofacial anomalies requires the cooperation of baby's parents with a number of specialists (e.g. plastic surgeons, maxillofacial surgeons, otolaryngologists, speech therapists, psychologists, orthodontists, dentists, audiologists, and others) until patient's adulthood (Edwards et al., 2007).

After the reparative surgeries, growing children are still confronted with various obstacles complicating their development. These issues vary for different age groups but they have to be dealt with in time to enable normal socialization and growth (Habel et al., 1996).

In the preschool age, patients and children face potential trouble with speech and language development leading to speech disorders. They are results of various factors, such as structural anomalies (e.g. velopharyngeal insufficiency) or associated dental and hearing problems. Additionally, factors affecting healthy normally developing children, also affect the speech development of cleft patients, e.g. environmental and emotional influences. A common speech disorder is hypernasality. Hearing problems can be caused by otitis media effusion (OME), fluid present in the middle ear, which is almost always present in children with a cleft palate (Dhillon, 1988). Palatal surgery manages to reduce the incidence of OME, but a continuous cooperation with an ENT (ear, nose and throat) surgeon is necessary. Cleft patients are suffering from various persisting orthodontic aberrations (Peterka, 1984). Proper dental care is needed as cleft patients are more prone to dental occlusions, but an orthodontic intervention is performed only when the permanent dentition is established.

In schoolchildren, the care is focused on alveolar bone grafting (handled surgically), orthodontic treatment, and psychology. Young children are susceptible to poor self-esteem, forming social relationships may be difficult for them and that can lead to depression (Habel et al., 1996). Good aesthetic results of surgery can be of great help for developing healthy self-esteem.

Adolescents may need to undergo a surgical procedure to correct the advancement of maxilla, and rhinoplasty, plastic surgery of the nose.

## 2.2 First surgery in patients with clefts

Primary cheiloplasty is a suture of soft tissues of the lip. It is the first surgery in patients with a cleft lip (both unilateral and bilateral) and serves to establish normal lip function and to reconstruct the nose (Cassell et al., 2009). It is performed before palatoplasty, closure of the

palate in cleft palate patients. Generally, surgeons prefer to perform the intervention at least at the age of 3 months, in the age between 3 and 6 months (Lee and Kim, 2003; Weatherley-White et al., 1987). Nonetheless, the timing of the first surgery is an open, widely debated topic. Many studies are dedicated to the question of the safest timing, but a clear, definite answer has not yet been found. In the end, the choice depends on various factors and surgeons' preferences.

### 2.2.1 Timing of the surgery

The ideal time for the operation is by many considered to be around the range of 6–12 weeks and surgeons use various factors to determine the exact timing, e.g. weight and the amount of haemoglobin (Lewin, 1964). The level of haemoglobin is highest at birth thanks to foetal haemoglobin which starts to decrease around 2–3 months of age. The rule of tens states that in order to perform the surgery with minimal risk to life, the baby should weigh at least 10 pounds, have a level of haemoglobin of at least 10 gm/dL and white blood cell count of less than 10,000 (Wilhelmsen and Musgrave 1966). These requirements are usually fulfilled at the age of 2–3 months when the lip has also grown enough in size. Not following the rule of tens leads a five-fold rate of postoperative complications. A modification of this rule is the rule of over 10: weight over 10 pounds, haemoglobin over 10 gm/dL and age over 10 weeks (Millard, 1976). On the other hand, there is a long-standing belief that the first 24 hours after birth are optimal for the surgery if the infant is otherwise perfectly healthy (Cannon, 1967). Some believe the best is to perform cheiloplasty after birth as soon as possible, ideally during the first 2 weeks (Stark, 1968).

A higher rate of morbidity was not observed in a group of infants with CL operated on early (first week or 1–3 weeks) compared to a group operated on late (3 weeks to 3 months, or later) (Weatherley-White et al., 1987). To the contrary, the former group had significantly fewer complications (see *Fig. 4*). Early surgery might bring several other advantages as well, such as a positive psychological effect on the family and earlier breast or bottle feeding. Also, manipulating the infant's lip and premaxillary tissues is easier, they can be well moulded and there is also a possibility of reducing the need for further procedures to achieve or maintain alignment of the alveoli (Bromley et al., 1983). Only slightly increased morbidity was observed in comparison with later surgery. The most common complication was a wound separation, more common in the early operated group but also more often observed in patients who underwent bilateral lip repair. The frequency of respiratory complications did not differ

between the early and late operated infants. In conclusion, it is of great importance to observe patients well and for the surgeon, anaesthesiologist, and paediatrician to cooperate to fully benefit from early lip repair.

| Category | Complications | Percent |
|---|---|---|
| Perinatal | 2 of 26 | 7.7 |
| Early | 5 of 23 | 21.7 |
| Late | 6 of 34 | 17.6 |
| Very late | 3 of 17 | 17.6 |
| TOTAL (early complications) | | 14.2 |
| TOTAL (late complications) | | 17.6 |

* There were no deaths, and there were 16 complications.

*Fig. 4. A table of complications that have occurred in each group of patients. The summed percentage for early operated children is lower than for those operated on later (Weatherley-White et al., 1987).*

In terms of surgical outcome, the success rates of the early and late surgery (3 months) were rated very similarly (Goodacre et al., 2004). There was no significant difference in the evaluation of scar attractiveness for the early or late operated. These outcomes imply there is no significant advantage of neonatal surgery compared to surgery at 3 months. But neonatal cheiloplasty is believed to be a worthy method anyway due to its psychological impact on the parents and the fact that no increased risk of anaesthesia at an earlier age was confirmed (Galinier et al., 2008). Considering the same aesthetics and qualitative results are achieved as with the later operation, then when the procedure is performed by an experienced surgeon it might be beneficial in the end.

Surgery in infants brings benefits such as a positive psychological impact on the family and also better scar healing. However, one of the most important benefits may be a better occlusion of the dental arch. In those operated early with a unilateral cleft, the alveolar cleft gap is forming the correct position faster, because the lip works as a sphincter and the tongue pushes as an obturator. That aids moulding of the dental arch and results in faster alveolar cleft closure (see *Fig. 5.*) (Akin et al., 1991). That is not the case in lips repaired later. The explanation for this is based on how the sucking reflex functions in a new-born. For infants with delayed repair of the lip, sucking pushes forward the cleft alveolar margins in unilateral cases and the premaxilla in bilateral cases.

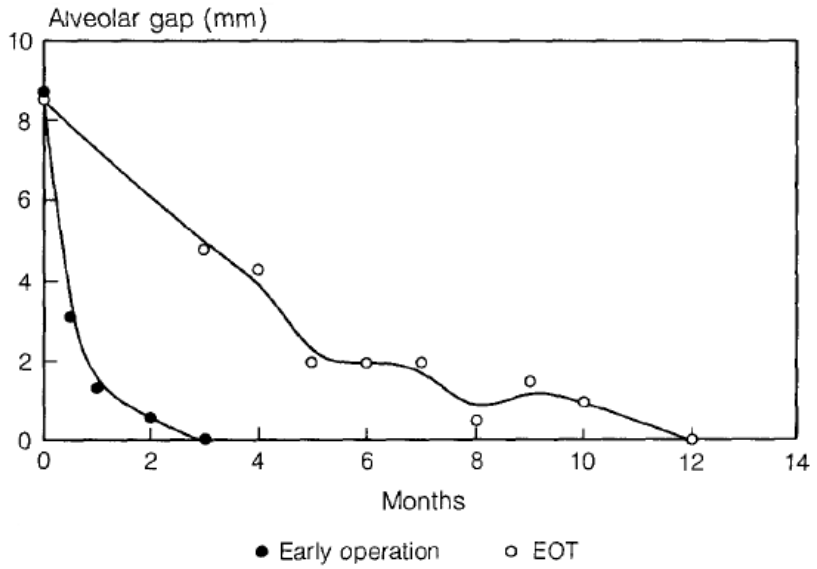


*Fig. 5. Monthly decrease of the alveolar gap in patients with unilateral cleft lip after early operation compared to the EOT patients. EOT – extraoral traction, a device used to apply force on the dentition in CLP patients (Akin et al., 1991).*

Neonatal cheiloplasty is considered safe by many, it does not carry greater risks than the delayed repair, and it may be recommended to all parents who prefer the surgery as soon as possible. Proper preoperative workup and postoperative follow-up are necessary, monitoring possible respiratory problems as those have been documented to threaten the infant the most. In another study, no complications due to anaesthesia were observed and breastfeeding was chosen as a feeding method for over 60% of the patients. A higher risk of surgical complications could appear in patients with bilateral cleft lip, but it can be avoided by a modification of the protocol (Harris et al., 2010).

Neonatal cheiloplasty is now a predominant method performed in the Czech Republic and the aesthetical and healing results are considered to be encouraging enough to favour early surgery compared to delayed repair protocols. The results so far have shown it may be necessary to perform small cosmetic corrections in approximately 25% of patients operated neonatally, compared to 26% in later operated patients (Borský et al., 2007). Positive psychologic impact and improved food intake are also included in the evaluation as key factors for the decision to favour early surgery protocol.

### 2.2.2 Protocols for lip cheiloplasty

There are various techniques used to suture the lip. They are usually either geometric repairs (e.g. Tennison) or rotation-advancement techniques (e.g. Millard, Mohler)

First complex protocols for lip repair started to appear in the 19$^{th}$ century. Works of von Graefe, who used incisions of the lip to achieve the cleft's closure by pairing the lip's edges, and Mirault. who used a flap from one horizontal incision and created a triangular flap which was used to overlap the cleft lip (Millard, 1976), served as starting point for many other authors. These techniques already yielded satisfying results, even though not very naturally looking, and the Cupid's bow, the double curve of the upper lip, was never reconstructed. LeMesurier (in *Fig. 6*) attempted to construct it artificially when he used a rectangular flap and turned it down and over (LeMesurier, 1949).

*Fig. 6. LeMesurier and Tennison repairs using a geometrical skin flap from the lateral aspect of the cleft. This solves the shortage on the medial cleft side and helps to restore the Cupid's bow, but both of these repairs disrupt the continuity of the philtral column (Marcus et al., 2017).*

A significant improvement was the geometric-style repair protocol for the unilateral cleft lip repair by the stencil method by Charles W. Tennison (Tennison, 1952). The peak in the margin of the cleft, a triangular flap, is used to reconstruct a natural Cupid's bow. Unfortunately, both Tennison's and LeMesuer's methods created a scar that disrupted face symmetry. Randall modified the Tennison method, still using the triangular flap but also combining several other different techniques. It maintains the normal Cupid's bow, and to construct the flap, tissue from the lateral side of the cleft is used, unlike other methods which often discard it. Randall also suggests the first 10 days of life for the operation (Randall, 1959).

Millard's rotation-advanced technique (*Fig. 7.*) maintains the continuity of the philtral column but philtral ridges may become asymmetric and meet. By adding a posterior incision to fix the appearance of the scar, Millard himself modified the method, now called the Millard II

technique (Millard, 1976). Unlike the previous approaches, this is not a geometric-style repair, which initially was not accepted, but eventually many modifications were developed, e.g. the very popular Mohler's modification.

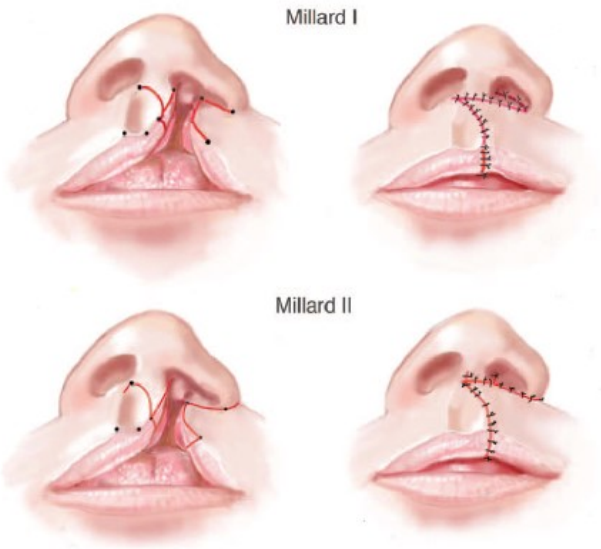


*Fig. 7. Millard I and Millard II repairs. Rotation-advancement intended to provide equal vertical lip lengths and a balanced Cupid's bow without disrupting the continuity of the philtral column (Marcus et al., 2017).*

According to the Mohler's protocol, the incision is lead higher and to create even philtral columns on both sides, clefted and non-clefted, additional tissue is used. This tissue is taken from the base of the columella, as visible in *Fig. 8*. The scar leads in parallel with the philtral column on the side of the cleft (Mohler, 1987).

A more modern method is the Fisher repair, which solves some of the issues associated with rotation-advancement protocols. The scars along the columella, nasal base and ala are avoided all together, and equal vertical length of the philtral ridges is created by using an inferior cutaneous triangle (Fisher, 2005).

The repair of bilateral cleft lip was initially approached in the same way as the repair of cleft lip – first one side was corrected and then the other. But bilateral clefts are often symmetrical (both clefts are complete, or incomplete), and this approach destroys the symmetry. Cheiloplasty of both sides at the same time is possible after premaxillary projection is corrected by preliminary labial adhesion. When dealing with asymmetric bilateral clefts (one cleft is complete, the other is not), it is possible to first perform preliminary labial or nasolabial adhesion, which sets a transitional phase of the bilateral incomplete cleft lip to establish symmetry and it can be progressed with cheiloplasty. One of the most used

techniques for bilateral cleft lip, based on this principle, is the Mulliken's repair (Mulliken, 2000).

Nasal deformity is present even in incomplete clefts and is preferably corrected directly when the lip repair is performed.

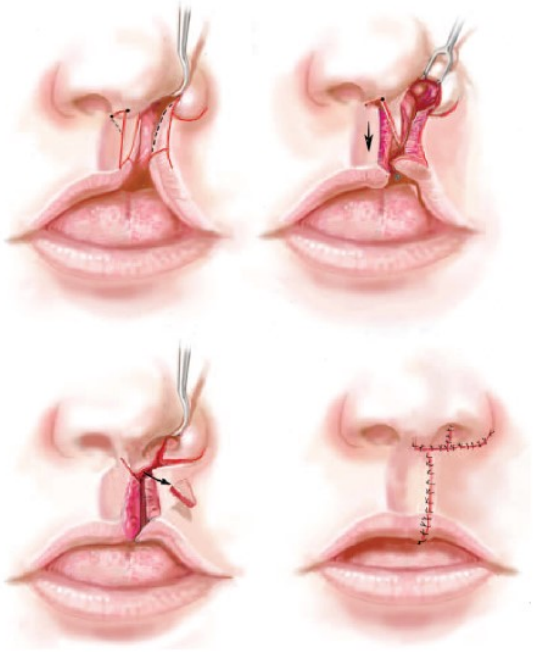

*Fig. 8. Mohler repair. The rotation incision is initiated higher, within the columella. The back-cut is extended to the apex of the normal philtral column which allows for necessary rotation while creating a philtral column originating at the lateral aspect of the cleft-side columella (Marcus et al., 2017).*

The key part of any technique is to achieve as natural-appearing philtral columns as possible, with a symmetrical Cupid's bow and the least disturbing scar. The success of each protocol depends greatly on the technical skill of the surgeon and on the chosen repair design. The selected method should result in only one lip repair surgery being sufficient until adulthood. The choice of the ideal repair method varies according to the cleft extent and particular type (Marcus et al., 2017). The guidelines for cleft lip surgery are shown below in *Table 1*.

*Table 1. Guiding Principles for Repair of Unilateral and Bilateral Cleft Lip (adapted from Marcus et al., 2017).*

| | |
|---|---|
| Unilateral cleft lip repair: | |
| Design | Design a closure interface (scar) that closely mirrors the contralateral philtral ridge in shape and length |
| | Limit the total scar burden inherent in the design |
| Execution | Create a symmetric a natural Cupid's bow |
| | Match the volume of vermilion on each side of the cleft |
| | Restore muscular continuity such that normal lip movement result |
| | Create a labial culcus of normal depth |
| | Create a normal nasal floor, nasal sill, and alar base |
| | Centralize the columella and elevate the columella base |
| Bilateral cleft lip repair: | |
| Planning and preparation | Maintain (or establish) symmetry |
| | Prepare the projecting premaxilla |
| | Anticipate future changes that will occur with growth |
| Execution | Construct a full central lip using lateral labial elements and discard prolabial vermilion |
| | Deepen the gingivolabial sulcus using premaxillary mucosa |
| | Establish muscular continuity primarily |
| | Address the nasal deformity synchronously |

### 2.2.3 Neonatal cheiloplasty

Neonatal cheiloplasty is the first lip surgery performed shortly after birth. According to this protocol, early surgery is more beneficial for an infant and the operation is recommended as soon as possible, ideally in the first week of life. Healthy new-borns without additional developmental defects are in a great physical condition and their immune system is the strongest right after birth. Transplacental immunity may play an important role in the new-born's ability to undergo surgery without complications and accelerate maturing and healing

of the scar. The infants need to undergo general anaesthesia and prior to the surgery, they must be carefully examined by their paediatrician and anaesthesiologist. Only those patients without any additional health problems or developmental malformations can be referred for neonatal cheiloplasty.

### 2.2.4 Neonatal cheiloplasty in the Czech Republic

Neonatal cheiloplasty has been performed in the Czech Republic at the Faculty Hospital Motol in Prague since 2005 (Borský et al., 2007). Currently, it is the predominant method used for the repair of cleft lip in the Czech Republic, with promising results without further recorded complications. The modified Tennison triangular flap repair is used and its scheme is displayed in *Fig. 9*.

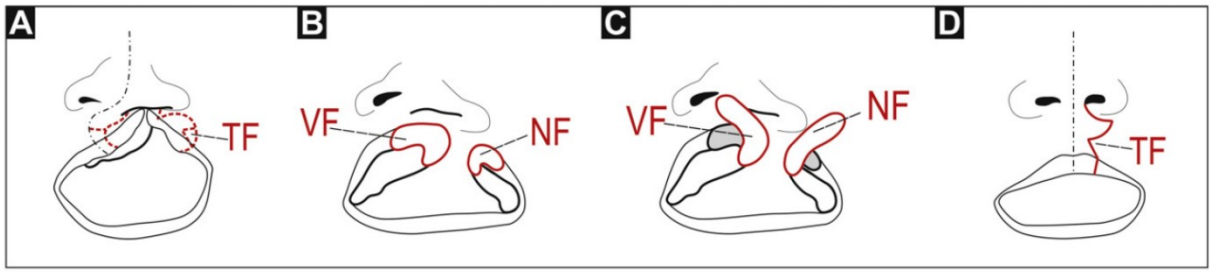


*Fig. 9. A surgical procedure based on the modified method of Tennison. (A) Cleft before cheiloplasty. Dotted lines show the planned surgical incisions including the position of the Tennison flap (TF). (B) A scheme of surgical incisions before elevating the flap for vestibule deepening (VF) and the flap for deepening the base and side parts of the nasal passage (NF). These flaps are outlined in the red line. (C) View showing the elevated tissue flaps VF and NF. The grey areas correspond to the original position of the VF and NF. (D) Enface aspect after the surgery. A scheme shows the post-operative scar and straightening of the midline (black hatch line), which was deviated before operation (A) (Borský et al., 2012).*

## 2.3 Benefits of neonatal cheiloplasty

### 2.3.1 Wound healing and aesthetic quality

Scar evaluation did not reveal any statistically significant difference in the aesthetic quality of the lip repair when comparing groups operated on early and late (Weatherley-White et al., 1987). In fact, in the early group, there was a slightly higher need for corrective surgery, but that more likely depends on the cleft type and severity, than on the timing of surgery. When children after early and late protocol (operation at 3 months of age) were compared, there

were no benefits gained from the early repair. Neither attractiveness nor surgical outcome was rated as better (Goodacre et al., 2004). A result of another comparison states the scar after neonatal surgery is cosmetically acceptable (Akin et al., 1991). On the contrary, other observations suggest possibly better aesthetic outcomes after the first surgery.

Right after birth, new-borns without other developmental defects are in a great physical and psychologic condition. Studies evaluating aesthetical results of cheiloplasty state better healing and physical appearance of the scar after neonatal cheiloplasty compared to surgery performed later in life. Few days old infants are characterized by persisting foetal scarless wound healing, which works based on a different immunologic principle and is much faster than postnatal healing. Early operations may leave no scar at all, or only a minimal one (Mast et al., 1992). Thus, early repair can benefit from very limited or even no scarring. In later repair, the situation is different. In new-borns, few days after birth, fibroblasts and keratinocytes differ from those in adults, which results in normal skin not being replaced with scar tissue (Krejčí et al., 2015). Based on a sample of facial tissue from a cleft, the fibroblasts differ subtly also between neonates and older children. Therefore, healing and scar maturing proceeds faster after neonatal cheiloplasty than after late operation (Živicová et al., 2017).

Observation of scar healing showed faster maturing in neonatally operated children (3–4 days) compared with the commonly used protocol for operation at the age of 3 months (7–8 days). After 8–12 months the scar is completely healed and not visible (Borský et al., 2012). Early repair showed great aesthetical quality of the scar and nose symmetry (Borský et al., 2007; McHeik et al., 2006)

### 2.3.2 Social factors and psychological burden on the family

Mothers of children born with orofacial clefts reportedly experience negative emotions more often, compared to those with healthy children (Brantley and Clifford, 1980). Mothers tend to experience anxiety, confusion, helplessness, stress and even refusal when it comes to forming of a loving bond with their child. Parents might feel embarrassed to show their offspring to their family and they are uncomfortable to talk about the malformation. It is easier to cope for those parents who know the diagnosis antenatally as they have time to research information and are provided specialist counselling and are therefore psychologically prepared (Davalbhakta and Hall, 2000; Matthews et al., 1998). Early surgery at the request of the mother is reported to have positive effects on their psychology and the integration of a baby into the family (McHeik and Levard, 2006). Conversely, other authors did not observe any

measurable difference in the psychologic conditions of mothers of children operated neonatally and those with children operated at 3 months (Slade et al., 1999). Mothers of those operated later performed alike in the psychologic analysis compared to the other group, simply due to having more time to process the infant's condition. Yet, many mothers preferred an earlier operation and expressed more satisfaction afterwards, while many from the later-operated group expressed regret that they should have opted for the early operation. Thus, even though their emotional condition was improving as well, mothers who had to wait for the operation experienced anticipatory anxiety, distress in going out in the public with their infant and a greater unsatisfaction with the result of the operation.

Neonatal cheiloplasty enables parents to leave the hospital with a healthy-looking child whose scar is healed and who can be fed more easily because the baby can establish sucking reflex. This gives parents time to reconcile with the baby´s condition and explain the health situation to their close family. Family and the baby itself are spared of the shock of their relatives and baby can be socially incorporated right after birth.

After the lip repair surgery, patients can be negatively psychologically affected and feel disapproved by society, because of their facial appearance. Children operated in the first week of life perform better in physical functioning and especially in self-esteem compared to a group of children operated at the age of several months (Petráčková et al., 2015). Although, in other evaluated characteristics (e.g. mental health, bodily pain, parental emotional impact), the groups perform similarly.

### 2.3.3 Feeding, improved growth and development

Patients with orofacial clefts are challenged with feeding difficulties right after birth. Feeding is even harder for patients with cleft palate than for cleft lip patients, as they are not able to generate a strong enough pressure (Reid et al., 2006). This may lead to reduced weight gain, compared with healthy new-borns.

The chosen method of feeding plays a part in how the infant grows. A commonly recommended method after the first surgery is feeding by a cup or a syringe with a short soft tube attached to its nozzle as to not stress the freshly operated structures. Both bottle feeding and breastfeeding were formerly either discouraged or not even taken into consideration. Bottle feeding should not pose risk after the cheiloplasty but may not provide any actual nutritional advantage compared to the other methods, like spoon-feeding (Assunção et al.,

2005). However, alternative methods of feeding may stress the infants and cause them to cry more often. A possible reduction in weight gain is documented when alternative methods of feeding are used compared to breastfeeding (Bessell et al., 2011). Also, as there is no risk to wound healing, unlike alternative methods, breastfeeding can start right after the repair (Matsunaka et al., 2019).

Some mothers choose to breastfeed their infants even after early lip surgery. An evaluation of the effects of breastfeeding on weight gain between cup-fed, bottle-fed, and breastfed groups, shows significantly better growth in the infants who are breastfed or bottle-fed to those who are cup-fed (*Fig. 10.*) (Weatherley-White et al., 1987). The tendency of improved growth applied also to infants who are switched from breastfeeding to a bottle. Considering the nutritional, psychologic, and immunologic benefits of breastfeeding and the fact that no postoperative complications or changes in the scar appearance were shown in breastfed infants compared to cup-fed children, it is possible to say that mothers who want to breastfeed their baby should be encouraged. Feeding using a bottle or even breastfeeding was shown to be without any complications or threat to the wound, so it can simplify and improve the postoperative phase and can start directly after the intervention (Cohen et al., 1992). Even though the improved growth in breastfed babies may not be statistically significant, it is still clearly more economical compared with the alternative methods (e.g. spoon-feeding) (Darzi et al., 1996).

| Category | 1-Month Gain | 3-Month Gain |
|---|---|---|
| Breast-feeders | 28% | 67% |
| Cup-feeders | 16% | 50% |

*Fig. 10. Weight gain observed in patients with cleft lip only after the surgery, the difference between breast-feeders and cup-feeders (Weatherley-White et al., 1987).*

Based on the statistics, cleft lip patients after neonatal surgery are breastfed at a similar rate compared to the general population (Burianova et al., 2017). In a group of early operated patients with cleft lip and palate, the ratio was found to be below the general population. Unfortunately, data used for the research did not include patients operated on later.

### 2.3.4 Reduced stay at the hospital

When neonatal cheiloplasty is performed, parents can leave the hospital in a week after the surgery, which sometimes does not exceed the standard length of hospital stay after childbirth

of a healthy baby. At that time, the scar is almost healed, and the baby can be fed normally. The infant looks healthy and provides the family enough time to reconcile with the baby´s condition.

Patient's stay in hospital is not prolonged for much compared to healthy new-borns and they leave the hospital already healed, on average 3–5 days after the procedure (Borský et al., 2012). Also, breastfed infants compared to those fed by a cup tend to stay in the hospital for a shorter time (Weatherley-White et al., 1987). Shorter stay not only means a reduced burden on the family but also a reduction in the hospital cost (Eaton et al., 1994). Shorter stay is not increasing the mortality and morbidity in children after cleft lip operations.

## 2.4 Possible risks of neonatal cheiloplasty

### 2.4.1 Anaesthesia in infants

Unclear neurologic effect of anaesthetic drugs used in early surgery on children raises many concerns when it comes to paediatric surgery. The impact on behavioural and neurological development is suspected yet not supported unanimously. The developing brain is extremely sensitive to even small and brief stimuli, if applied in a crucial period. Anaesthetic agents work as these stimuli by way of strongly modulating neurotransmitter signalling. Cheiloplasty is performed extremely early and under general anaesthesia, which makes it debatable whether it is appropriate for a freshly born infant.

If the infants are gestationally mature and healthy, they can be recommended for neonatal cleft lip repair and no increase in complications due to anaesthesia is observed (Stephens et al., 1997). However, neonates, in general, are at higher risk of hypoxia or apnoea after anaesthesia, thus it is important to pay attention to any possible respiratory distress in the postoperative period. A higher rate of post-operative complications in preterm infants operated on in the first months of life has been reported, particularly in those with lower body weight (compared to mature and premature patients) at the time of the surgery (Steward, 1982). It is necessary to carefully monitor such patients in the first hours after anaesthesia, as there is a high risk of respiratory complications, mainly apnoea. Premature patients with a previous history of apnoea prior to the anaesthesia, are more prone to its recurrence, even compared with a group of prematurely born infants without previously recorded respiratory complications (Liu et al., 1983). If the infants at risk are carefully examined and identified prior to surgery, anaesthesia itself is not a cause of post-operative complications.

Concerning paediatric anaesthesia, many questions need to be further researched. Even if the particular types of anaesthetic agents are approved and commonly used, they should be re-examined to make sure they are safe for paediatric practice (Nasr and Davis, 2015).

#### 2.4.1.1 Brain development and IQ impairment

Studies in animals have shown serious neurotoxic effects of anaesthetic agents on the adult brains of rats (Jevtovic-Todorovic et al., 2000), developing brains of rodents (Anand and Soriano 2004; Olney et al. 2004; Olney et al. 2002), and cognitive function in adult animals after neonatal exposure (Loepke and Soriano, 2008). This leads to a serious concerns regarding whether it is harmful to perform surgery under general anaesthesia in human new-borns. The existence of a "window of vulnerability", when the brain of a neonate is more susceptible to impairment was clearly identified in animal studies but there is no conclusive evidence proving its presence in human neonates. If this period of higher susceptibility to neurotoxic impairment in humans exists, it could be until up to 3 years of age (Sun, 2010).

It is a complex issue to filter out confounding variables, which might affect or add to a potentially harmful effect of anaesthesia. The outcome may be affected by exposure to various drugs during pregnancy and after delivery, and by environmental or ecological characteristics. The clinical manifestation of anaesthesia neurotoxicity, if it exists at all, seems to be very subtle. As much concern as it causes, there is very little evidence supporting it (Hansen et al., 2011; Vutskits et al., 2012). New data needs to be collected and if the need is there, anaesthesia practice needs to change accordingly.

The incidence of developmental or behavioural disorders in children who underwent surgery with general anaesthesia before the age of 3 was found to be more than twice as high as in the control group (DiMaggio et al., 2009). The evidence for a relationship to anaesthesia at an early age was however not conclusive and the same applies to results of other studies. A sibling-controlled analysis supports a 60% higher risk of developmental/behavioural disorders for children who underwent surgery before the age of 3 years but the answer to the question of whether is it attributable to anaesthesia stays uncertain (DiMaggio et al., 2011). An analysis of previous papers dealing with the influence of anaesthesia came to the conclusion, that the concerns over possible anaesthetic neurotoxicity are justified and there is epidemiologic evidence supporting them, yet clear indications are still missing (DiMaggio et al., 2012). There is good evidence that children who undergo more than one surgery in general anaesthesia before the age of 4 years, are almost at twice the risk of developing learning

disabilities later in life (Wilder et al., 2009). This risk increases with the number of interventions and their cumulative duration. One exposure does not supposedly increase this risk. It is not only difficult to determine whether there are significant consequences of anaesthetic exposure in children but also how much the actual age of the first exposure influences the development of behavioural disturbances later in life. Children who underwent some kind of surgery early in life (aged 0–6 months) were found to be suffering from behavioural disruptions more often than children operated at the age older than 2 years (Kalkman et al., 2009). However, these results are still not statistically significant. For retrospective studies to be fully reliable, much bigger populations of patients are required.

Other studies disprove the hypothesis of neurocognitive impairment. Data acquired from the Netherlands Twin registry showed that exposed twins had more cognitive problems than unexposed twins. But an unexposed co-twin performed similarly to their exposed co-twin (Bartels et al., 2009). Comparison of academic performance of Danish 9$^{th}$ graders did not provide stable evidence for neurologic impairment as children who underwent short anaesthesia at neonatal age did not perform worse than their peers (Hansen et al., 2011). If an early exposure even leads to clinically measurable deficits, clear evidence of neurotoxicity is still not supported by evidences (Olsen and Brambrink, 2013). A reason for why it might be difficult to determine the actual influence of anaesthesia on neurological development lies within how the studies are designed. They tend to be retrospective, nonuniform, evaluating only small populations of patients and lacking key pieces of information about some of the characteristic of anaesthesia that can be highly variable (Sun, 2010). The length of anaesthesia, anaesthetics used, the kind of surgery – all of these can be confounding factors.

No significant difference was found when the intelligence quotient of children at the age of 3–7 years, who were operated on for cleft lip in their first year of life but with different timing (first week or the age of several months) was compared (Petráčková et al., 2015). These results do not make it clear, whether there is a negative impact on IQ before the age of 3 years but conclude that timing of cheiloplasty into the first week of life should not be a cause of IQ impairment. In all cases, sevoflurane was used to induce and maintain anaesthesia. Sevoflurane ensures a good quality of anaesthesia and performs better when compared to halothane, formerly regularly used paediatric anaesthetic (Redhu et al., 2010). Sevoflurane induces anaesthesia much faster and works more reliably (fewer cardiac arrhythmias, cough, apnoea and movement), shows fewer postoperative complications (e.g. nausea, vomiting) and recovery occurs faster.

### 2.4.2 Growth and development of palate

Patients with cleft lip and palate suffer from maxillofacial abnormalities, manifested mainly as a deficiency of midfacial growth and developmental defects of hard and soft tissues (Eppley et al., 2005; Marazita and Mooney, 2004). The maxilla is affected by disturbances in growth, which is very notable especially in those suffering from complete unilateral clefts (Smahel and Brejcha, 1983). The impact of cleft lip and palate repair will probably be ever present. The severity of growth impairment is depending on the extent of original cleft and also on the technique used to repair cleft lip because that could decide the pressure exerted on the alveolar arch (Shi and Losee, 2015).

It is documented, that early lip closure can in fact favour the formation of the dental arches, due to an early adjustment of the orbicularis oris muscle. The alveolar arches help especially in cleft patients because the alveolar-palatal cleft is reduced faster (Bardach and Eisbach, 1977). It was later confirmed again that lip pressure after the repair acts as a major effector of the craniofacial growth. (Bardach, 1990). Lip repair supposedly enhances the dimensions of maxillary width and height, posterior facial width, and mandibular length, but it inhibits maxillary length.

Early lip repair could be responsible for a major decrease in alveolar cleft width and anterior arch depth caused by a pressure generated by the lip, on the anterior maxillary arch after cheiloplasty (Huang et al., 2002). The measured landmarks are shown in *Fig. 11*., dimensions for which these landmarks are used are shown in the *Table 2*. In a group of patients with unilateral complete cleft lip and palate operated on average at 3.2 months with the Millard's rotation-advancement technique, the alveolar cleft width growth decreased significantly in the periods between 3–6 and 6–12 months. Also, lower growth in the intercanine width of the maxillary arch (decreased significantly after the 6$^{th}$ month) and anterior arch depth (decreased after the 3$^{rd}$ month) was measured. Up to the age of 12 months, there were no significant effects observed either on the posterior dimensions of the dental arch or linear growth of the maxillary anterior segments. Similar effects on the reduction of the alveolar cleft width were reported before, neonatal repair should not lead to any impairment of facial growth compared to later repair (Christie et al., 1991). Therefore, when the positive psychological impact and lower frequency of middle ear diseases are taken into consideration, neonatal repair as a whole may be more beneficial in the long run. The neonatally repaired lip is said to have a formative effect which helps to close the cleft gap in the palate (Velemínská et al., 2018).

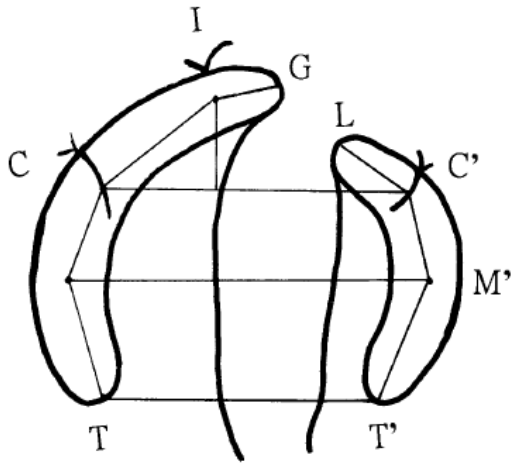


*Fig. 11. A diagram of the maxillary dental cast with landmarks used for linear and angular measurements. These landmarks were defined according to Mazaheri et al. (1971) (Huang et al., 2002).*

After early lip closure, the alveolar cleft width reduces as well, which aids the restoration and symmetry of the dental bony arch (Eichhorn et al., 2011). Although, in this study the operation performed at the age of 3–6 months is considered to be the early protocol, thus the demonstrated positive effect should be valid for what is otherwise considered as the late surgery. Lip repair is also said to have a greater impact in reducing the anterior arch width and length compared to presurgical orthopaedics which does not result in a statistically significant change in the arch dimensions (Adali et al., 2012).

When evaluating the effect of the early lip repair compared to the late repair (at 3 months), the early one has several advantages, including improved aesthetics of the face, speech development, and eating. But most importantly, an objectively positive contribution of the early repair is that on the development of the anterior segment of the dentoalveolar arch. A repaired lip can create pressure on the frontal segment much sooner, which aids natural development (Valentová-Strenáčiková and Malina, 2016). These findings correspond with those of Huang et al.

In general, the pressure of a repaired lip is acknowledged by various studies as a contributing factor in reducing the alveolar cleft width. But it seems it is actually the moulding effect of the repaired lip combined with the growth of the anterior ends of the upper jaw (Hoffmannova et al., 2016). Importantly, the growth of maxilla of patients after neonatal cheiloplasty was more similar to the noncleft control group to those from later operation repair group. In a one year follow up of patients after neonatal cheiloplasty, there was no actual reduction observed

in the length or width dimensions. The alveolar cleft was narrowed thanks to the formative effect of the repaired lip placed on the growing anterior parts of the upper dental arch (Hoffmannova et al., 2018).

*Table 2. Linear dimensions and angular measurements measured on the dental casts (adapted from Huang et al., 2002).*

| | |
|---|---|
| G-L | alveolar cleft width |
| I-G | anterior portion of nonclefted segment |
| I-C | anterior ridge length of nonclefted segment |
| L-C′ | anterior ridge length of clefted segment |
| C-C′ | intercanine width |
| M-M′ | middle arch width |
| T-T′ | intertuberosity width |
| I⊥CC′ | anterior arch depth |
| ∠GC-CC′ | anterior basal angle |
| ∠GIC | anterior arch curvature angle on nonclefted segment |

The development of facial morphology following early cheiloplasty is a vital issue because if should the patients be more prone to deviations affecting their later life, it could easily overweight any advantages gained by neonatal repair early in life. Preschool children (aged 3–4.5 years) with operated cleft lip compared with noncleft children show a major deviation of facial morphology (Dadáková et al., 2016). Disturbances of facial symmetry are more highlighted in older children, therefore differentiating between the effect of cheiloplasty and palatoplasty or other potential surgeries may not be possible. But when the adults with repaired lip and adults with repaired lip and palate were measured, the lip surgery alone was shown to give the same level of morphology disturbance as combined surgery (Capelozza Filho et al., 1996). Therefore, its influence on patients can be considered greater. The impact of neonatal cheiloplasty should not increase incidence of more severe deviations compared to those children operated on later (Dadáková et al., 2016). The impairment is more noticeable in the patients affected by unilateral or bilateral cleft lip and palate, their chin is more prominent than the one of the control group. That is potentially caused by the additive effect of the lip

and palatal surgery. But overall, the shapes of all operated groups are still in line with typical deviations of cleft patients, even of those with severe types. The differences in face symmetry between cleft patients and control group of similar age are nonetheless statistically significant and differs according to the cleft type (Moslerová et al., 2018). Patients with unilateral CL and UCLP showed greater asymmetry in the nasolabial area on the cleft side. Patients with BCLP were a bit more similar to the control group but the asymmetry was greater. Assymetries did not increase in the group of older patients, apart from asymmetry in buccal region, present in patients with BCLP and UCLP.

If the results of the dentoalveolar arch dimensions of 3 possible surgical time protocols are compared in patients with unilateral cleft lip and palate (UCLP), there are statistically significant differences in the growth of the sagittal length of the alveolar arch in patients undergoing neonatal lip surgery (Kotova et al., 2019). Casts of three groups of UCLP patients and one control group were measured and compared in intercanine width, intermolar width, and sagittal length of the alveolar arch. The first group underwent lip repair at the age of 6 months and palate repair at the age of 4 years. Second and third groups both underwent palate repair at the age of 9 months, but one group was operated according to an early lip repair protocol and the other at the age of 3 months. In the first two measurements, groups of UCLP patients were not significantly different, while in the latter one, the group treated according to the neonatal lip repair protocol showed a statistically significant difference compared to all other groups. That suggests that the pressure generated by the lip is somehow affecting the growth of sagittal length more in early operated patients. However, even the statistically significant results are not considered to be clinically significant. It is clear that more data from patients of more age groups needs to be collected.

### 2.4.3 Surgical requirements

At the time when neonatal cheiloplasty is performed, the separated parts of soft tissue are small. Some surgeons prefer to wait at least a few months to perform this surgery so that the infant can grow. Nonetheless, the growth of palatal bones and soft tissue in 3 months is not significant, as it is less than 2 mm of vertical height (Stark, 1968). The surgeon and the whole operational team must be skilled and there are high demands for post-anaesthesia care and monitoring of the infant.

# 3 Conclusion

In this review I attempted to cover information available on the topic of neonatal cheiloplasty as the first operation in patients with a cleft lip with or without a cleft palate. Despite years of practice and extensive research on cheiloplasty and issues associated with it, its optimal timing continues to be a topic of a debate. Considering the clefts are multifactorial developmental malformations affecting infancy, childhood, and adulthood of the patient, it is necessary to focus the attention on all the steps of the cleft managing process. Cheiloplasty as the first operation which patients undergo may have the potential to significantly influence further growth and psychological burden on the afflicted individual.

It was shown by multiple authors that patients operated early after birth heal more easily and their scars mature faster. A new-born infant is in a great condition, thanks to their transplacental immunity and altered fibroblast expression resulting in an almost or completely scar-less healing. Also, proper feeding can start directly after the surgery. Bottle feeding or breastfeeding does not pose any risk to the fresh wound, and it is more economical and beneficial for the baby than alternative methods. The sucking reflex can be established directly, and the risk that the baby will develop malnutrition is reduced.

The surgery has a significant positive psychologic influence on the family, mainly on the interaction between mother and her child. It is important for a baby with such a visible facial defect requiring years of treatment to be accepted by the family. The approach towards the baby can improve even the child's own emotional development as cleft patients are significantly more threatened by psychologic issues, low self-esteem, stigma, abuse and social disapproval. Early surgery reportedly offers psychological support, the parents can bring home a normally looking child and accept the malformation under less harsh conditions.

In the neonatal program, infants are operated dominantly in the first week of their life. That means, that a baby is exposed to general anaesthesia very early. Paediatric anaesthesia is a source of many disputes and uncertainties. Animals studied showed a clear neurotoxic influence on the developing brain. But for human neonates, no conclusive proof for the same effect was found. The so-called window of vulnerability could last even up to 3 years of life, if it exists at all in humans. Yet mortality and morbidity is not increased with lower age, and no IQ impairment or slower cognitive development was observed in children after neonatal surgery. However, more than one anaesthetic exposure has already been shown to result in a higher risk for the child. It seems that a key to safe anaesthesia is a meticulous care during the

operation and especially afterwards, as one of the biggest risks is posed by respiratory problems. But if only healthy infants properly evaluated before the surgery and without additional developmental abnormalities are chosen, the surgery is safe. Paediatric anaesthesia still requires further studies, individual anaesthetic agents and their influence need to be re-examined, but so far, no harm is considered to affect the infants undergoing neonatal surgery.

Another question of a great importance tied closely to cheiloplasty performed at any age, is its effect on facial growth and morphology. Patients with facial clefts usually have to undergo some correctional surgeries later in life, as well as orthodontic interventions. Should alveolar development be disrupted, this could easily overweight the positive effects of neonatal repair. So far, no negative effect of neonatal cheiloplasty was measured to be clinically significant. Repaired lip supposedly works in favour of the palate and helps to close the cleft, if it is present. It is also possible that after neonatal cheiloplasty, fewer patients need to undergo further corrective surgical repair. Although it has been shown that clefts always cause facial asymmetry and it is necessary to evaluate the effect of neonatal repair.

It is clear there are still many issues requiring more research. Whether it is paediatric anaesthesia, facial development, or the psychological impact on the child. Many authors agree, that the positive effects of scar maturation, more effective feeding, and acceptance of the child are important factors that outweigh the risks that so far have not been directly proven. If the family after the counselling asks for it, neonatal corrective surgery should be provided to a cleft patient. It is necessary that a carefully chosen protocol for the surgery is performed by skilled a medical team with an experienced surgeon and that the infant is closely monitored afterwards. Until a direct disadvantage or risk of the neonatal repair is demonstrated, early repair should continue to be recommended as the preferred option.

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